IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Bernd RIEDL et al. In re Application of: Serial No.: 09/889,227 Group Art Unit: 1625 Filed: January 8, 2002 Examiner: Rita J. Desai Ω-CARBOXYARYL SUBSTITUTED DIPHENYL UREAS AS RAF KINASE For: INHIBITORS INFORMATION DISCLOSURE STATEMENT UNDER 37 CFR §§ 1.56, 1.97 and 1.98 Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450 Sir: This information disclosure statement is made in accordance with 37 C.F.R. §§ 1.56, 1.97 and 1.98 as follows: Timing and Fees Under 37 C.F.R. § 1.97(b), no fee or statement is required for filing this information X disclosure statement is filed: within three months of the filing date of a national application other than a CPA under § 1.53(d); within three months of the actual filing date of the national phase of a PCT application; OR X. before the mailing of a first substantive office action (including after filing of an RCE). Under 37 C.F.R. § 1.97(c), this information disclosure statement is filed after the periods specified in 37 C.F.R. § 1.97(b), but before the mailing date of:

> a final rejection under 37 C.F.R. 1.113; termination of prosecution, e.g. Ex Parte Quayle, M.P.E.P § 609(B)(2); OR a notice of allowance under 37 C.F.R. § 1.311; and

		is acco	ompanied by:
			the statement as specified in 37 C.F.R. § 1.97(e) set out below; OR
			a check covering the fee of \$180.00 under 37 C.F.R. § 1.17(p).
			R. § 1.97(d), this information disclosure statement is filed after the mailing lowing actions which have not been withdrawn:
		a final	action under 37 C.F.R. § 1.113;
		termin	ation of prosecution, e.g. Ex Parte Quayle, M.P.E.P § 609(B)(2);
		OR a r	notice of allowance under 37 C.F.R. § 1.311;
	AND i	is filed	on or before payment of the issue fee; AND is accompanied by:
			tement as specified in 37 C.F.R. § 1.97(e) as set forth below, and the fee of 00 under 37 C.F.R. § 1.17(p).
Staten	nents Ui	nder 3 <u>7</u>	C.F.R. 1.97(e)
			Each item of information contained in this information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application having a mailing date not more than three months prior to the filing date of this information disclosure statement; or
			No item of information contained in this information disclosure statement was cited in a communication from a foreign patent office in a counterpart foreign application, and to the knowledge of the undersigned attorney after making reasonable inquiry, no item of information contained in this information disclosure statement was known to any individual designated in 37 C.F.R. § 1.56(c) more than three months prior to the filing date of the information disclosure statement.
Cited :	<u>Materia</u>	<u>ls</u>	
		ancesto	of materials listed but not attached were cited in benefit (35 U.S.C. § 120) or application Serial No, on Form 892 by the Examiner and/or Form y the applicant; see 37 C.F.R. § 1.98(d).
		_	of materials listed but not attached were cited in an international search dated
	\boxtimes	Not rec	quired by 37 CFR § 1.98.
	\boxtimes	Copies	of the materials listed are attached (except for the foregoing).

Non-F	inglish l	Language References
		An English-language search report or equivalent paper from a foreign patent office is provided indicating the relevance of the cited reference(s).
		A foreign-language search report from a foreign patent office is provided, and pertinent parts are translated substantively below:
		 X = document of particular relevance when it is taken alone Y = document of particular relevance when it is combined with another such document
		A = document defining the general state of the art O = non-written disclosure
		P = intercalated document
		T = document cited to understand the theory or principle underlying the invention
		E = patent document which has the benefit of a date earlier than the filing date and which was published only on or after this filing date
		D = cited in the application
		L = cited for another reason
		& = publication of member of same patent family
		Translation of other relevant information on foreign search report
		[insert necessary translation here]
Other	Informa	<u>ution</u>
Payme	nt of Fe	es Due (If Any):
	A chec	ck for \$ covering the fee identified above is attached.
	Please	charge to Deposit Account No. 13-3402 \$ for the fee identified above.

The Commissioner is hereby authorized to charge or credit any overpayment to Deposit Account #13-3402, two copies of this paper are attached for this purpose.

Respectfully submitted,

Csaba Henter, Reg. No. 50,908 Attorney/Agent for Applicants

MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
Arlington Courthouse Plaza l
2200 Clarendon Blvd. Suite 1400
Arlington, Virginia 22201
Telephone: (703) 243-6333
Facsimile: (703) 243-6410

,

Date: May 24, 2006

CH:pdr

Attorney Docket No.: BAYER-0015-A

PTO/SB/08A (08-00)

Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet of

	Complete if Known	1
Application Number	09/889,227	
Filing Date	January 8, 2002	
First Named Inventor	Bernd RIEDL et al.	
Group Art Unit	1625	
Examiner Name	Rita J. Desai	
Attorney Docket Number	BAYER-0015-A	

			U.S. P	ATENT DOCUMENTS	,
Examiner Initials *	Cite No.1	U.S. Patent Docum	ent Kind Code ² (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY
	A1	2002/0173507	A1	Santora et al.	11-21-2002
. "	A2	2002/0065283	A1	McMahon et al.	05-30-2002
	А3	2002/0065296	A1	Dumas et al.	05-30-2002
	A4	2004/0209905	A1	Kubo et al.	10-21-2004
	A5	5063247		Sekiya et al.	11-05-1991
	A6	5151344		Abe et al.	09-29-1992
	A7	5658903		Adams et al.	08-19-1997
	A8	5710094		Minami et al.	01-20-1998
	A9	5559137		Adams et al.	09-24-1996
· · · · · ·	A10	5808080		Bell et al.	09-15-1998
	A11	6297381	B1	Cirillo et al.	10-02-2001
	A12	6310068	B1	Böttcher et al.	10-30-2001
	A13	6329415	B1	Cirillo et al.	12-11-2001
	A14	6358945	B1	Breitfelder et al.	03-19-2002
	A15	6372773	B1	Regan	04-16-2002
	A16	6492393	B1	Breitfelder et al.	12-10-2002
	A17	6525046	B1	Cirillo et al.	02-25-2003
	A18	6583282	B1	Zhang et al.	06-24-2003
	A19	6608052	B2	Breitfelder et al.	08-19-2003
	A20	3284433		Becker et al.	11-08-1966
	A21	4546191		Nishiyama et al.	10-08-1985
	A22	6380218		Marfat et al.	04-30-02
	A23	6500863		Qi et al.	12-31-2002

FOREIGN PATENT DOCUMENTS									
		Foreign Patent Document			Date of Publication of	Pages, Columns, Lines, Where Relevant			
Examiner Initlals*	Cite No.1	Office ³	Number ⁴	Kind Code ⁵ (<i>if known</i>)	Name of Patentee or Applicant of Cited Document	Cited Document MM-DD-YYYY	Passages or Relevant Figures Appear	T ⁸	
	B1	wo	02/14311	A2	Amgen Inc.	02-21-2002			
	B2	wo	02/32872	A1	Eisai Co. Ltd.	04-25-2002			
	B3	wo	02/44158	A1	Pfizer Products Inc.	06-06-2002			
	B4	wo	02/07772	A2	Boehringer Ingelheim	01-31-2002			
	B5	wo	01/04115	A2	Boehringer Ingelheim	01-18-2001			
	В6	wo	99/62890	A1	Pfizer Products Inc.	12-09-1999			

Examiner Signature		Date Considered	

Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO Complete if Known Application Number 09/889,227 INFORMATION DISCLOSURE Filing Date January 8, 2002 STATEMENT BY APPLICANT First Named Inventor Bernd RIEDL et al. Group Art Unit 1625 (use as many sheets as necessary) Examiner Name Rita J. Desai BAYER-0015-A Sheet of Attorney Docket Number

			FOR	REIGN PA	TENT DOCUMENTS (co	nt'd)	-	
Examiner Initials*	Cite No.1	Office ³	Foreign Patent Docum Number ⁴	ent Kind Code⁵ (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁶
	B7	JP	01200254	A2	Hirabayashi Shigeto	08-11-1989		
	B8	JP	01102461	A2	Hirabayashi Shigeto	04-20-1989		_
	В9	JP	01259360	A2	Hirabayashi Shigeto	10-17-1989		_
	B10	JP	01009455	A2	Megumi et al.	01-12-1989		
	B11	JP	06075172	B4	Megumi et al.	09-07-1988		
	B12	JP	06120039	A2	Hideki	10-02-1992		_
	B13	JP	03144634	A2	Shigeto et al.	06-20-1991		
	B14	JP	03198049	A2	Jiro et al.	12-27-1989		_
	B15	JP	02150840	A2	Toshihiko et al.	06-11-1990		
	B16	JP	02105016	A2	Hideo et al.	04-17-1990		
	B17	JP	02108048	A2	Minoru et al.	04-19-1990		
	B18	JP	02035450	A2	Toshihiko et al.	07-26-1988		
	B19	WO	00/50425	A1	Boehringer Ingelheim	08-31-2000		
	B20	W	98/34929	A1	Smithkline Beecham	08-13-1998		
	B21	W	98/32439	A1	Smithkline Beecham	07-30-1998		
	B22	V	01/09088	A1	Kirin Beer Kabushiki	02-08-2001		
	B23	8	2005/048948	A2	Ambit Biosciences	06-02-2005		
	B24	wo	02/062763	A2	Bayer Corporation	08-15-2002		
	B25	WO	02/083628	A1	Boehringer Ingelheim	10-24-2002		_
	B26	WO	02/085857	A2	Bayer Corporation	10-31-2002		
	B27	WO	02/085859	A1	Bayer Corporation	10-31-2002		
	B28	wo	97/09973	A2	Univ. of California	03-20-1997		
	B29	wo	03/068229	A 1	Bayer Corporation	08-21-2003		
	B30	WO	03/068746	A 1	Bayer Corporation	08-21-2003		
	B31	wo	03/099771	A2	Novartis AG	12-04-2003		
	B32	wo	03/082272	A1	Chiron Corp.	10-09-2003		
	B33	WO	02/059102	A2	Aventis Pharma	08-01-2002		

Examiner Signature	· · · · · · · · · · · · · · · · · · ·	Date Considered	

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered, include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached. Number refers to English language corresponding family member.

Approved for use through 10/31/2002. OMB 0651-0031 U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO Complete if Known Application Number 09/889,227 INFORMATION DISCLOSURE January 8, 2002 Filing Date STATEMENT BY APPLICANT Bernd RIEDL et al. First Named Inventor Group Art Unit 1625 (use as many sheets as necessary) Rita J. Desai Examiner Name BAYER-0015-A of Sheet Attorney Docket Number

			FOR	EIGN PA	TENT DOCUMENTS (con	ıt'd.)		
Examiner Initials*	Cite No.1	Office ³	Foreign Patent Docum Number ⁴	ent Kind Code ^s (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	Τ°
	B34	WO	01/07411	A1	Banyu Pharmaceutical	02-01-2001		
	B35	UK	1110099		Julia	06-07-1966		
	B36	WO	2004078746	A2	Boyer et al.	09-16-2004		
	B37	wo	2005037273	A1	Ramurthy et al.	04-28-2005		
	B38	wo	2005037285	A1	Ramurthy et al.	04-28-2005		
	B39	wo	2005049603	A1	Finsinger et al.	06-02-2005		
	B40	wo	2005019192	A1	Hoelzemann et al.	03-03-2005		
	B41	WO	2004043374	A2	Anderson et al.	05-27-2004		
	B42	wo	2005042520	A1	Staehle et al.	05-12-2005		
	B43	wo	2005037829	A1	Staehle et al.	04-28-2005		
	B44	wo	2005004864	A1	Buchstaller et al.	01-20-2005		
· ·	B45	wo	2004037789	A2	Buchstaller et al.	05-06-2004		
	B46	wo	2005047283	A1	Hoelzemann et al.	05-26-2005		
	B47	WO	2005002673	A1	Gill et al.	01-13-2005		
	B48	wo	02059081	A2	Hocker et al.	08-01-2002		
	B49	wo	2005004863	A1	Buchstaller et al.	01-20-2005		
	B50	wo	2005032548	A1	Amiri et al.	04-14-2005		
	B51	wo	2004085425	A1	Dipietro et al.	10-07-204		
	B52	WO	0055152	A1	Cirillo et al.	09-21-2000		
·	B53	WO	0157008	A1	Cusack et al.	08-09-2001		
	B54	wo	2005058832	A1	Finsinger et al.	06-30-2005		
	B55	wo	2005005389	A2	Bruge et al.	01-20-2005		
	B56	wo	2004085399	A1	Buchstaller et al.	10-07-2004		
	B57	wo	02083642	A1	Breitfelder et al.	10-24-2002		
	B58	wo	0071532	A1	Gant et al.	11-30-2000		
-	B59	wo	0210141	A1	Ahliganian et al.	02-07-2002		

Examiner Signature		Date Considered		
-----------------------	--	--------------------	--	--

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁶ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached. Number refers to English language corresponding family member.

PTO/SB/08A (08-00)

Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet of

	Complete If Known
Application Number	09/889,227
Filing Date	January 8, 2002
First Named Inventor	Bernd RIEDL et al.
Group Art Unit	1625
Examiner Name	Rita J. Desai
Attorney Docket Number	BAYER-0015-A

			FOF	REIGN PA	TENT DOCUMENTS (con	nt'd.)		
Examiner	Cite No.1			ent Kind Code ⁶ (if known)	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T ⁵
	B60	WO	0214281	A1	Cochran et al.	02-21-2002	, , <u>g</u>	
	B61	wo	2004019941	A1	Buchstaller et al.	03-11-2004		
	B62	wo	0035454	A1	Ko et al.	06-22-2000		
,	B63	wo	0104115	A2	Zhang et al.	01-18-2001		
	B64	wo	0218346	A1	Cooper et al.	03-07-2002		
	B65	wo	0026203	A1	Pevarello et al.	05-11-2000		
	B66	wo	0043366	A1	Kirin et al.	07-27-2000		
	B67	wo	0056331	A1	Stamos et al.	09-28-2000		
	B68	wo	9820868	A1	Tracey et al.	05-22-1998		
	B69	WO	9203413	A1	Lythgoe et al.	03-05-1992		
•	B70	wo	03047523	A2	Lyons et al.	06-12-2003		
	B71	wo	03068228	A1	Dumas et al.	08-21-2003		
	B72	wo	02092576	A1	Cirillo et al.	11-21-2002		
	B73	wo	9845268	A1	Marfat et al.	10-15-1998		
	B74	EP	1256587	A1	Omura et al.	11-13-2002		
	B75	EP	1199306	A1	Hayama et al.	04-24-2002		
	B76	EP	0709225	B1	Minami et al.	08-05-1998		
,	B77	EP	0425443	A1	Oechslein et al.	05-02-1991		
	B78	EP	0690344	A1	Sugita et al.	01-03-1996		
	B79	wo	9928305	A1	Walker	06-10-1999		• •

NON PATENT LITERATURE DOCUMENTS					
Examiner Initials *					
	C1 Nickel et al., "Carboxylic acid analogues of suramin, potential filaricides," <i>Indian Journal of Chemistry</i> , Vol. 30B, February 1991, p. 182-187				
C2 Duam et al., "The ins and outs of Raf kinases," TIBS 19, November 1994, p. 474-480.					
	C3	Campbell et al., "Increasing complexity of Ras signaling," Oncogene, (1998) 17, 1395-1413			
Bolton et al., "Ras oncogene directed approaches in cancer chemotherapy," Annual Reports in Medicinal Chemistry, 29, pp. 165-174					
	C5	Moelling et al., "Signal transuction as target of gene therapy," Institute of Medical Virology, University of Zürich, Recent Results in Cancer Research, Vol. 142, pp. 63-71			

	Examiner Sìgnature		Date Considered	
--	-----------------------	--	--------------------	--

Sheet

of

+

Approved for use through 10/31/2002. OMB 0651-0031 U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

BAYER-0015-A

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Attorney Docket Number

Substitute for form 1449A/PTO

Complete If Known

Application Number 09/889,227

Filing Date January 8, 2002

First Named Inventor Bernd RIEDL et al.

Group Art Unit 1625

(use as many sheets as necessary)

Rita J. Desai

		NON PATENT LITERATURE DOCUMENTS (cont'd.)	
Examiner initials *	Cite No.1	include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	
	C6	Jay H. Stein, Internal Medicine, 4 th Edition, 1994, pp. 699-715	
	C7	Johannes L. Bos, "Ras oncogenes in human cancer: a review," Cancer Research, 49, 4682-4689, September 1, 1989	
	C8	Kempter et al., "Synthese potentieller Pflanzenschutz- und Schädlingsbekämpfungsmittel aus substituierten Anilinen," Pädagosische Hochschule, Eingegangen am 1.7.1982, 101-120	
	C9	Lyons et al., "Discovery of a novel Raf kinase inhibitor," Endocrine-Related Cancer, (2001) 8, 219-225	
	C10	Lowinger et al., "Design and discovery of small molecules targeting Raf-1 kinase," Current Pharmaceutical Design, 2002, 8, 2269-2278	
	C11	Dumas et al., "Recent developments in the discovery of protein kinase inhibitors from the urea class," Current Opinion in Drug Discovery & Development, 2004, 7(5):600-616	
	C12	Dumas, "Protein kinase inhibitors from the urea class," Current Opinion in Drug Discovery & Development, 2002, 5(5):718-727	
	C13	Lowinger et al., "Discovery of novel class of potent Raf kinase inhibitors: structure activity relationships," Clinical Cancer Research, Vol. 6, Nov. 2000, 4533s	
	C14	Hotte et al., "BAY 43-9006: Early Clinical Data in Patients with Advanced Solid Malignancies," Current Pharmaceutical Design, 2002, 8, 2249-2253	
	C15	Lee et al., "BAY-43-9006: Bayer/Onyx," Current Opinion in Investigational Drugs, 2003, 4(6):757-763	
	C16	Sorbara et al., "BAY-43-9006," <i>Drugs of the Future</i> , 2002, 27(12):1141-1147 - Oncolytic Raf Kinase Inhibitor.	•
	C17	Khire et al., "Omega-carboxypyridyl substituted ureas as raf kinase inhibitors: SAR of the amid substituent," <i>Bioorg. Med. Chem. Lett.</i> , 14 (2004), 783-786	
	C18	Wilhelm et al., "BAY 43-9006 Exhibits broad spectrum oral antitumor activity and targets the RAF/MEK/ERK pathway and receptor tyrosine kinases involved in tumor progression and angiogenesis," Cancer Research, 64, 7099-7109, October 1, 2004	
İ	C19	Smith, et al., "Discovery of heterocyclic ureas as a new class of raf kinase inhibitors: identification of a second generation lead by a combinatorial chemistry approach." Bioorganic & Medicinal Chemistry Letters, 11 (2001) 2775-2778	
	C20	Bankston et al., "A scaleable synthesis of BAY 43-9006: a potent raf kinase inhibitor for the treatment of cancer." Organic Process Research & Development, 2002, 6, 777-781	_

Examiner Signature		Date Considered	
	I		

treatment of cancer," Organic Process Research & Development, 2002, 6, 777-781

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ¹ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached. Number refers to English language corresponding family member.

<u></u>

Approved for use through 10/31/2002. OMB 0651-0031 U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of Information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet	6	of	10

Complete if Known			
Application Number	09/889,227		
Filing Date	January 8, 2002		
First Named Inventor	Bernd RIEDL et al.		
Group Art Unit	1625		
Examiner Name	Rita J. Desai		
Attorney Docket Number	BAYER-0015-A		

		NON PATENT LITERATURE DOCUMENTS (cont'd.)	
Examiner Initials *	Cite No.1	include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	C21	Strumberg et al., "Results of phase I pharmacokinetic and pharmacodynamic studies of the raf kinase inhibitor BAY 43-9006 in patients with solid tumors," <i>International Journal of Clinical Pharmacology and Therapeutics</i> , Vol. 40, No. 12/2002 (580-581)	
	C22	Chang et al., "BAY 43-9006 (Sorafenib) inhibitors ectopic (s.c.) and orthotopic growth of a murine model of renal adenocarcinoma (Renca) predominantly through inhibition of tumor angiogenesis," 96 th Annual Meeting, April 16-20, 2005, Anaheim/Orange County, CA	
	C23	Panka et al., "BAY 43-9006 induces apoptosis in melanoma cell lines," 96th Annual Meeting, April 16-20, 2005, Anaheim/Orange County, CA	
	C24	Auclair, et al., "BAY 43-9006 (Sorafenib) is a potent inhibitor of FLT3 tyrosine kinase signaling and proliferation in AML cells," 96 th Annual Meeting, April 16-20, 2005, Anaheim/Orange County, CA	
	C25	Murphy et al., "BAY 43-9006 controls tumor growth through inhibition of vascular development," 96 th Annual Meeting, April 16-20, 2005, Anaheim/Orange County, CA	
	C26	Spronsen et al., "Novel treatment strategies in clear-cell metastatic renal cell carcinoma," Anti-Cancer Drugs, 2005, 16:709-717	
	C27	Thaimattam et al., "3D-QSAR CoMFA, CoMSIA studies on substituted ureas as Raf-1 kinase inhibitors and its confirmation with structure-based studies," <i>Bioorganic & Medicinal Chemistry</i> , 12(2004) 6415-6425	
,	C28	Danson et al., "Improving outcomes in advanced malignant melanoma," <i>Drugs</i> , 2005, 65(6):733-743	
	C29	Heim et al., "Antitumor effect and potentiation or reduction in cytotoxic drug activity in human colon carcinoma cells by the Raf kinase inhibitor (RKI) BAY 43-9006," International Journal of Clinical Pharmacology and Therapeutics, Vol. 41, No. 12/2003 (616-617)	
	C30	Richly et al., "Results of a phase I trial of BAY 43-9006 in combination with doxorubicin in patients with primary hepatic cancer," <i>International Journal of Clinical Pharmacology and Therapeutics</i> , Vol. 42, No. 11/204 (650-651)	
	C31	Mross et al., "Drug-drug reaction pharmacokinetic study with the Raf kinase inhibitor (RKI) BAY 43-9006 administered in combination with irinotecan (CPT-11) in patients with solid tumors," International Journal of Clinical Pharmacology and Therapeutics, Vol. 41, No. 12/2003 (618-619)	
	C32	Richly et al., "A phase I clinical and pharmacokinetic study of the Raf kinase inhibitor (RKI) BAY 43-9006 administered in combination with doxorubicin in patients with solid tumors," International Journal of Clinical Pharmacology and Therapeutics, Vol. 41, No. 12/2003 (620-621)	

Examiner Signature		Date Considered		
-----------------------	--	--------------------	--	--

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached. Number refers to English language corresponding family member.

+

Approved for use through 10/31/2002. OMB 0651-0031 U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet	7	of	10

	Complete if Known
Application Number	09/889,227
Filing Date	January 8, 2002
First Named Inventor	Bernd RIEDL et al.
Group Art Unit	1625
Examiner Name	Rita J. Desai
Attorney Docket Number	BAYER-0015-A

		NON PATENT LITERATURE DOCUMENTS (cont'd.)	
Examiner Initials *	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T 2
	C33	DeGrendele, "Activity of the raf kinase inhibitor BAY 43-9006 in patients with advanced solid tumors," Clinical Colorectal Cancer, May 2003, pp. 16-18	
	C34	Hubbard, "Oncogenic mutations in B-Raf: some losses yield gains," Skirball Institute of Biomolecular Medicine and Department of Pharmacology, New York University School of Medicine, New York, NY	
	C35	Thompson et al., "Recent progress in targeting the Raf/MEK/ERK pathway with inhibitors in cancer drug discovery," Curr. Opin. Pharmacol., 2005 Aug., 5(4):350-6	
	C36	Moore et al., "Phase I study to determine the safety and pharmacokinetics of the novel Raf kinase and VEGFR inhibitor BAY 43-9006, administered for 28 days on/7 days off in patients with advanced, refractory solid tumors," <i>Annals of Oncology</i> , 16:1688-1694, 2005	
	C37	Ahmad et al., "Kinase inhibition with BAY 43-9006 in renal cell carcinoma," Clinical Cancer Research, Vol. 10, 6388s-6392s, 15 Sept. 2004	
	C38	Wan et al., "Mechanism of activation of the RAF-ERK signaling pathway by oncogenic mutations of B-RAF," <i>Cell</i> , Vol. 116, 855-867, 19 March 2004	
	C39	Hanson, "Pulmonary-Allergy, Dermatological, Gastrointestinal & Arthritis, Inhibitors of p38 kinase," Exp. Opin. Ther. Patents, (1997) 7(7):729-733	
	C40	Strumberg et al., "Phase I clinical and pharmacokinetic study of the novel raf kinase and vascular endothelial growth factor receptor inhibitor BAY 43-9006 in patients with advanced refractory solid tumors," <i>Journal of Clinical Oncology</i> , Vol. 23, No. 5, 10 Feb. 2005, 965-972	·
	C41	Regan et al., "Pyrazole urea-based inhibitors of p38 MAP kinase: from lead compound to clinical candidate," <i>J. Med. Chem.</i> , 2002, 45, 2994-3008	
	C42	Clark et al., "Safety and pharmacokinetics of the dual action raf kinase and vascular endothelial growth factor receptor inhibitor, BAY 43-9006, in patients with advanced, refractory solid tumors," Clin. Cancer Res., 2005:11(15), 1 August 2005, 5472-5480	
	C43	Wilson et al., "The structural basis for the specificity of pyridinylimidazole inhibitors of p38 MAP kinase," <i>Chemistry & Biology</i> , 1997, Vol. 4, No. 6, 423-431	
	C44	Jeffcoat et al., "The metabolism and toxicity of halogenated carbanilides," <i>Drug Metabolism and Deposition</i> , Vol. 5, No. 2, 157-166	
	C45	Murata et al., "Facile synthesis of new pyrrolo[3,4-d]pyrimidine-2,4-diones," Chem. Pharm. Bull., 22(5) 1212-1213 (1974)	

Examiner Signature		Date Considered	
-----------------------	--	--------------------	--

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁵ Applicant is to place a check mark here if English language Translation is attached. Number refers to English language corresponding family member.

+

Approved for use through 10/31/2002. OMB 0651-0031 U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO Complete if Known 09/889,227 **Application Number** INFORMATION DISCLOSURE Filing Date January 8, 2002 STATEMENT BY APPLICANT First Named Inventor Bernd RIEDL et al. Group Art Unit 1625 (use as many sheets as necessary) **Examiner Name** Rita J. Desai Sheet of BAYER-0015-A Attorney Docket Number

	NON PATENT LITERATURE DOCUMENTS (cont'd.)					
Examiner Initials * Cite No.1		Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.				
	C46	Iwadate Y. et al, "Intra-arterial ACNU, CDDP chemotherapy for brain metastases from lung cancer: comparison of cases with and without intra-arterial mannitol infusion," <i>Neurol. Surg.</i> , (1993) vol. 21, no. 6, pp. 513-518				
	C47	Hanson, "Inhibitors of p38 kinase," Expert Opinion on Therapeutic Patents, July 1997, vol. 7, no. 7, pp. 729-733(5)				
	C48	Garcia-Lopez et al., "New routes for the synthesis of pyrrolo[3,2-d]- and -[2,3-d]pyrimidine systems starting from a common pyrrole derivative," <i>Journal of the Chemical Society</i> , Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1978), (5), 483-7				
	C49	Wilhelm et al., "BAY 43-9006: preclinical data," Curr Pharm Des, 2002, 8(25):2255-7				
	C50	Wright et al., "Clinical trials referral resource. Current clinical trials of BAY 43-9006, Part 1," Oncology, 2005 Apr, 19(4):499-502				
	C51	Dumas, "Protein kinase inhibitors from the ureas class," Current Opinion in Drug Discovery & Development, 2002, Vol. 5, No. 5, 718-727				
	C52	Patent Abstracts of Japan, Publication No. 02-023337, published 01-28-1990				
	C53	Patent Abstracts of Japan, Publication No. 02-022650, published 01-25-1990				
	C54	Wissner et al., "Analogues of platelet activating factor. 7. Bis-aryl amide and bis-aryl urea receptor antagonists of PAF," <i>J. Med. Chem.</i> , 1992, 35, 4779-4789				
	C55	Ravi et al., "Activated raf-1 causes growth arrest in human small cell lung cancer cells," <i>J. Clin. Invest.</i> , pp. 153-159				
	C56	Lemoine, "Overview of ras oncogenes and their clinical potential," Chapter 10,				
	C57	Drug, facts and comparisons, 1994 Edition, pp. 2703-2705				
	C58	Siu et all, "Phase I study of oral raf-1 kinase inhibitor BAY 43-9006 with gemcitabine in patients with advanced solid tumors," <i>Proc Am Soc Clinic Oncol</i> , 22:207, 2003 (abstr 828)	•			
	C59	Escudier et al., "Randomized phase III trial of the raf kinase and VEGFR inhibitor sorafenib (BAY 43-9006) in patients with advanced renal cell carcinoma (RCC)," Meeting: 2005 ASCO Annual Meeting, Category: Genitourinary Cancer, Subcategory: Kidney Cancer, Abstract No. 4510				
	C60	Eisen et al., "Phase I trial of BAY 43-9006 (sorafenib) combined with dacarbazine (DTIC) in metastatic melanoma patients," Meeting: 2005 ASCO Annual Meeting, Category: Melamona, Subcategory: Melamona, Abstract No. 7508				

Examiner Signature		Date Considered	
-----------------------	--	--------------------	--

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WiPO Standard ST. 18 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached. Number refers to English language corresponding family member.

Approved for use through 10/31/2002. OMB 0651-0031
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid CMB control number.

Substitute	for form 1449A/PTC)		Complete If Known		
				Application Number	09/889,227	
INFO	RMATION	DIS	CLOSURE	Filing Date	January 8, 2002	
STAT	TEMENT B	Y AI	PPLICANT	First Named Inventor	Bernd RIEDL et al.	
				Group Art Unit	1625	
	(use as many she	ets as	necessary)	Examiner Name	Rita J. Desai	
Sheet	9	of	10	Attorney Docket Number	BAYER-0015-A	

		NON PATENT LITERATURE DOCUMENTS (cont'd.)	
Examiner Initials *	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	C61	Adjel et al., "A phase I study of BAY 43-9006 and gefitinib in patients with refractory or recurrent non-small-cell lung cancer (NSCLC)," Meeting: 2005 ASCO Annual Meeting, Category: Developmental Therapeutics: Molecular Therapeutics, Subcategory: Antiangiogenic or Antimetastatic agents, Abstract No. 4510	
	C62	Carling et al., "1-(3-cyanobenzylpiperidin-4-yl)-5-methyl-4-phenyl-1,3-dihydroimidazol-2-one: A selective high-affinity antagonist for the human dopamine D ₄ receptor with excellent selectivity over ion channels," <i>J. Med. Chem.</i> , 1999, 42, 2706-2715	
	C63	Van Muijlwijk-Koezen et al., "Isoquinoline and quinazoline urea analogues as antagonists for the human adenosine A ₃ receptor," <i>J. Med. Chem.</i> , 2000, 43, 2227-2238	
	C64	Eisenhauer et al., "Impact of new non-cytotoxics in the treatment in ovarian cancer," Int. J. Gynecol Cancer, 2001, 11 (Suppl. 1), 68-72	
	C65	Kubo et al., "Synthesis and structure-activity relationship of quinazoline-urea derivatives as novel orally active VEGF receptor tyrosine kinase selective inhibitors," #913, XP-001152608	
_	C66	Carter et al, "Anti-tumor efficacy of the orally active raf kinase inhibitor BAY 43-9006 in human tumor xenograft models," #4954, XP-001145482	
	C67	Strumberg et al., "Phase I and pharmacokinetic study of the raf kinase inhibitor bay 43-9006 in patients with locally advanced or metastatic cancer," #2921, XP-001145481	
	C68	Dumas et al., "1-phenyl-5-pyrazolyl ureas: potent and selective p38 kinase inhibitors," Bioorganic & Medicinal Chemistry Letters, 10 (2000), 2051-2054	
	C69	Riedl et al., "Potent raf kinase inhibitors from the diphenylurea class: structure activity relationships," #4956, XP-001145518	
	C70	Iwadate et al., "Intra-arterial ACNU, CDDP chemotherapy for brain metastases from lung cancer: comparison of cases with and without intra-arterial mannitol infusion," Dept of Neurological Surgery, Chiba Cancer Center Hospital, Clinical Trial, Journal Article, Randomized Controlled Trial, Vol. 21, No. 6, 513-518	
	C71	Geiger et al., "Antitumor activity of a C-raf antisense oligonucleotide in combination with standard chemotherapeutic agents against various human tumors transplanted subcutaneously into nude mice," Clinical Cancer Research, Vol. 3, 1179-1185, July 1997	
	C72	Cunningham et al., "A phase I trial of H-ras antisense oligonucleotide ISIS 2503 administered as a continuous intravenous infusion in patients with advanced carcinoma," Cancer, September 2001, Vol. 92, No. 5, 1265-1271	
	C73	Madwed et al., "Pharmacological Evaluation of BIRB 796, a selective inhibitor of P38 MAP Kinase (MAPK), in animal models of endotoxic shock, inflammation and arthritis," Inflammation Res., 50:S184, 2001.	
·	C74	Blanco, "p38 MAPK signaling cascades: ancient roles and new functions," Bioassays, 22:637-645, 2000	

Examiner Signature		Date Considered		
-----------------------	--	--------------------	--	--

Approved for use through 10/31/2002. OMB 0651-0031 U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO Complete if Known Application Number 09/889,227 INFORMATION DISCLOSURE Filing Date January 8, 2002 STATEMENT BY APPLICANT First Named Inventor Bernd RIEDL et al. Group Art Unit 1625 (use as many sheets as necessary) **Examiner Name** Rita J. Desai Sheet of Attorney Docket Number BAYER-0015-A

	OTHER PRIOR ART NON PATENT LITERATURE DOCUMENTS					
Examiner Initials *	Cite No.1	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T 2			
	C76	Redman, A. M.; Johnson, J. S.; Dally, R.; Swartz, S.; Wild, H.; Paulsen, H.; Caringal, Y.; Gunn, D.; Renick, J.; Osterhout, M.; Kingery-Wood, J.; Smith, R. A.; Lee, W.; Dumas, J.; Wilhelm, S. M.; Housley, T. J.; Bhargava, A.; Ranges, G. E.; Shrikhande, A.; Young, D.; Bombara, M.; Scott W. J. "P38 Kinase Inhibitors for the Treatment of Arthritis and Osteoporosis: Thienyl, Furyl and Pyrrolyl Ureas" Bioorg. Med. Chem. Lett. 2001, 11 (1), 9.				
	C77	Dumas, J.; Hatoum-Mokdad, H.; Sibley, R. N.; Smith, R. A.; Scott, W. J.; Khire, U.; Lee, W.; Wood, J.; Wolanin, D.; Cooley, J.; Bankston, D.; Redman, A. M.; Schoenleber, R.; Caringal, Y.; Gunn, D.; Romero, R.; Osterhout, M.; Paulsen, H.; Housley, T. J.; Wilhelm, S. M.; Bhargava, A.; Pirro, J.; Chien, DS.; Ranges, G. E.; Shrikhande, A.; Muzsi, A.; Bortolon, E.; Wakefield, J.; Gianpaolo-Ostravage, C.; Chau, T. "Synthesis and Pharmacological Characterization of a Potent, Orally Active p38 Kinase Inhibitor" Bioorg. Med. Chem. Lett. 2002, 12, 1559.				
	C78	Dumas, J. "Protein Kinase Inhibitors from the Urea Class" Curr. Opin. Drug Discov. Dev. 2002, 5(5), 715-724.				
	C79	Dumas, J.; Sibley, R.; Riedl, B.; Monahan, MK.; Lee, W.; Lowinger, T. B.; Redman, A. M.; Johnson, J. S.; Kingery-Wood, J.; Scott, W. J.; Smith, R. A.; Bobko, M.; Schoenleber, R.; Ranges, G. E.; Housley, T. J.; Bhargava, A.; Wilhelm, S. M.; Shrikhande, A. "Discovery of a New Class of p38 Kinase Inhibitors" Bioorg. Med. Chem. Lett. 2000, 10 (18), 2047.				
	C80	Proceedings of the American Association for Cancer Research - Volume 42 - March 2001 - #4957 A Novel Diphenylurea Raf-1 Kinase Inhibitor (RKI) Blocks the Raf/Mek/Erk Pathway in Tumor Cells. Scott McClelland Wilhelm et al., Bayer Corporation.				

f			
Examiner		Date	
		24.0	1
Signature		Considered	
[Oignataro	ł.	Odiloladica	

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chlef Information Officer, U.S. Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, DC 20231.



¹ Unique citation designation number. ² Applicant is to place a check mark here if English language Translation is attached.